UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,769	07/21/2003	Birol Emir	109536.182	4223

26694 7590 02/08/2008

VENABLE LLP
P.O. BOX 34385
WASHINGTON, DC 20043-9998

EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
02/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,769	EMIR ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7 and 10-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7 and 10-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted October 31, 2007 wherein claims 3-7, 11-17, and 19-23 are amended. This application claims priority to foreign application JP2002-363139, filed December 13, 2002.

Claims 3-7 and 10-23 are pending in this application.

Claims 3-7 and 10-23 as amended are examined on the merits herein.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 18, 2007 has been entered.

Applicant's amendment, submitted May 18, 2007, with respect to the rejection of instant claims 14-17 and 22-23 under 35 USC 112, first paragraph, for introducing new matter into the claims, has been fully considered and found to be persuasive to remove the rejection as the rejected claims no longer recite the unsupported limitation. Therefore the rejection is withdrawn.

Applicant's arguments and amendment, submitted May 18, 2007, with respect to the rejection of instant claims 3-7 and 10-23 under 35 USC 103(a) for being obvious

over US patent 5100901, has been fully considered and found to be persuasive to remove the rejection as one of ordinary skill in the art would not have expected that administration of donepezil would stabilize or improve the cognitive score, such as the SIB, of a patient having severe Alzheimer's disease. Therefore the rejection is withdrawn.

Applicant's arguments and amendment, submitted May 18, 2007, with respect to the rejection of instant claims 3-7 and 10-23 under 35 USC 103(a) for being obvious over US patent 4895841, has been fully considered and found to be persuasive to remove the rejection as one of ordinary skill in the art would not have expected that administration of donepezil would stabilize or improve the cognitive score, such as the SIB, of a patient having severe Alzheimer's disease. Therefore the rejection is withdrawn.

Applicant's arguments and amendment, submitted May 18, 2007, with respect to the rejection of instant claims 3-7 and 10-23 under the doctrine of obviousness-type double patenting for claiming the same invention as claims 9-10 of US patent 5100901, has been fully considered and found to be persuasive to remove the rejection as one of ordinary skill in the art would not have expected that administration of donepezil would stabilize or improve the cognitive score, such as the SIB, of a patient having severe Alzheimer's disease. Therefore the rejection is withdrawn.

Applicant's arguments and amendment, submitted May 18, 2007, with respect to the rejection of instant claims 3-7 and 10-23 under claims 3-7 and 10-23 under the doctrine of obviousness-type double patenting for claiming the same invention as claims 12-13 of US patent 4895841, has been fully considered and found to be persuasive to remove the rejection as one of ordinary skill in the art would not have expected that administration of donepezil would stabilize or improve the cognitive score, such as the SIB, of a patient having severe Alzheimer's disease. Therefore the rejection is withdrawn.

The following rejections of record in the previous office action are maintained:

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-7 and 10-23 are rejected under 35 U.S.C. 102(b) as being unpatentable over Feldman et al. (of record in previous action) Feldman et al. discloses a study of the efficacy of donepezil for the treatment of moderate to severe Alzheimer's disease, characterized by a score of 5-17 on the Folstein Mini-Mental State Exam. (p. 614, left column, third paragraph) This range of scores fully includes the limitations of claims 3, 4, and 9. (a score of 5-9) The dose administered to the patients was either 5 or 10 mg

per day, (p. 614, left column, first paragraph) both of which fall within the dose limitations of claims 3, 6, 7, 11, 12, and 19-21. The dose was administered at 5 mg/day for 4 weeks, then increased to 10 mg per day, in a dosing regimen which was identical to that of instant claim 13. With respect to the period of time "sufficient to show improvement or no reduction in a cognitive function, recited in instant claims 3-5, the specification does not explicitly define this period, but the only period of time discussed in the specification is 24 weeks. (See the example on pp. 18-24 of the specification as amended) Therefore this time limitation is interpreted as at least including 24 weeks as a sufficient period of time. P. 614, left column, paragraph 1 of Feldman et al. discloses that the therapeutic method of Feldman et al. was carried out for 24 weeks, thus anticipating this limitation. The method of Feldman et al. involves administering the same compound in the same dose to the same or similar patient population. Although it is not mentioned whether the patient's MMSE or other cognitive scores improved or remained constant during the treatment, as disclosed in instant claims 14-17, this outcome is considered to be inherent in the method of Feldman et al., as the steps disclosed in the reference are the same as in the instant claims, administering the same compound in the same amounts to the same subjects by the same mode of administration. See *Ex parte Novitski* 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993). Note that the claiming of a new use, new function, or unknown property which is inherently present in the prior art does not make the claim patentable. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). See also *Eli Lilly and Co. v.*

Barr Laboratories Inc. 251 F3c. 955; 58 USPQ2d 1869-1881 (Fed. Cir. 2001) with regard to inherency as it relates to the claimed invention herein.

The claimed invention is thus anticipated by Feldman et al.

Response to Argument: Applicant's arguments, submitted May 18, 2007, with respect to the grounds of rejection discussed above, have been fully considered and not found to be sufficient to remove the rejection. Applicant argues that Feldman et al. does not disclose a step of specifically selecting a patient with a MMSE score of between 5-9. This argument is not convincing because anticipation of a range does not always depend on whether the prior art discloses a range with a mean falling within the claimed range. According to MPEP 2131.03, a reference may anticipate a claimed range in the absence of specific examples falling within the range if the claimed range is disclosed with sufficient specificity to constitute an anticipation under the statute. In the instant case, a range was disclosed which included patients with severe to moderate AD. (MMSE scores 5-17 as opposed to 5-9 in the claimed invention) The focus of this study was on the treatment of **moderate to severe** AD using donepezil, as opposed to previous studies which had focused on **mild to moderate** AD. (p. 613, right column, second paragraph) Mild to moderate AD, as described by prior studies, included a range of MMSE scores of 10-26, (p. 618, left column, fourth paragraph), as opposed to moderate to severe AD which is disclosed as encompassing MMAS scores of 5-17, indicating that Feldman et al. was operating with the same definition of "moderate" and "severe" AD disclosed by Applicant. Feldman et al. specifically observes that the disclosed results, "suggest that donepezil could be beneficial **for the symptomatic**

management of more advanced AD stages than those previously investigated." (p. 618, left column, third paragraph) In other words, the reference specifically discloses the lower end of the subject population (those with severe AD) as being of special interest in that this population was not previously known to benefit from donepezil. Therefore, the subset of experimental subjects having severe AD, with a MMSE score of 5 to 9, are disclosed with sufficient specificity to anticipate the claimed invention.

Applicant further argues that the patients of Feldman et al. having recognized severe Alzheimer's disease (MMSE 5-9) are not clearly disclosed by Feldman et al. to have actually improved as a result of the therapy. However, as discussed above, this outcome is an inherent property of the claimed method, as the method of Feldman et al. involves administering the same compound in the same amount to the same patients for the same duration as the claimed invention.

It is further noted that secondary considerations such as unexpected results or effects not reported in the prior art do not serve to overcome a showing of anticipation under 35 USC 102. Therefore the magnitude of the effect reported by Applicant will not serve to render the claimed invention patentable over the disclosure of Feldman et al.

For these reasons the rejection is maintained.

The following new grounds of rejection are introduced:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-7 and 10-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsolaki et al. (Reference includes with PTO-892) in view of Dooley et al. (Reference included with PTO-892) Tsolaki et al. discloses a study comparing acetylcholinesterase inhibitors and nootropics in patients with Alzheimer's disease. (p. 29, right column, paragraphs 3-4) The acetylcholinesterase inhibitors used were tacrine and donepezil. Patients were classified as having mild, moderate, or severe dementia, with severe dementia being a MMSE score of 0-10. (p. 30, left column last paragraph, right column first paragraph) Patients having severe Alzheimer's disease receiving acetylcholinesterase inhibitors exhibited a mean change of 2.67 on the MMSE score after 6 months (24 weeks) which is interpreted as the period of time "sufficient to show improvement or no reduction in a cognitive function, recited in instant claims 3-5, and used in the examples in the specification. (See the example on pp. 18-24 of the specification as amended) Tsolaki et al. does not disclose administering donepezil to a patient population having the exact MMSE range of 5-9, in a dose of 5 or 10 mg/day.

Dooley et al. discloses that he standard dose for administration of donepezil is 5 or 10 mg/day. (p. 200, paragraphs 1-2)

It would have been obvious to one of ordinary skill in the art at the time of the invention to use donepezil in the methods of Tsolaki et al. in a dose of 5 or 10 mg/day. One of ordinary skill in the art would have been motivated to use these doses because Dooley et al. discloses administration of donepezil for Alzheimer's disease in these

dosages. One of ordinary skill in the art would reasonably have expected success because determining the correct dosage and dosing schedule is well within the ordinary and routine level of skill in the art.

It would also have been obvious to one of ordinary skill in the art to select a patient having a MMSE score of 5-9. This range lies within the range recited by Tsolaki et al. When the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. See *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). See MPEP § 2144.05 [R-1].

Thus the invention taken as a whole is *prima facie* obvious.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson
Patent Examiner
AU 1623
2/1/08

Anna Jiang
2/6/08
Supervisory Patent Examiner
AU 1623